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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/606,745	06/27/2003	Peter Gluckman	704652-9001	5345

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EXAMINER	
RUSSEL, JEFFREY E	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/606,745	GLUCKMAN ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *78-92* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *78-92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/185,804.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. A request for continued examination under 37 CFR 1.114 was filed in this application after a decision by the Board of Patent Appeals and Interferences, but before the filing of a Notice of Appeal to the Court of Appeals for the Federal Circuit or the commencement of a civil action. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on October 13, 2009 has been entered.

2. The amendment to the specification filed June 28, 2007 does not accurately mark all changes made to the paragraph at column 1, lines 3-8, of U.S. Patent No. 5,714,460, as is required by 37 CFR 1.173(b)(1). In particular, at line 4 of the amended paragraph, the comma which originally appeared after "abandoned" has been omitted without the change being marked with brackets. At line 11 of the amended paragraph, "USC" has been changed to "U.S.C." without the change being appropriately marked. Correction is required, by submission of a new version of the amended paragraph, with all changes relative to the version of paragraph occurring in the '460 patent being accurately marked.

The amendment to the claims filed October 13, 2009 is not in compliance with 37 CFR 1.126 because the new claims were not numbered beginning with the number next following the highest numbered claim previously presented. Note that in the amendment filed June 28, 2007, the highest numbered claim present in the amendment was numbered "77". Accordingly, the new claims numbered "74" through "88" in the amendment filed October 13, 2009 have been re-numbered under 37 CFR 1.126 as "78" through "92", respectively. In the response to this Office action, Applicants must submit a new listing of claims in appropriate amendment format

showing the re-numbered claim numbers, and showing claim dependencies which are corrected in accordance with the claim re-numbering. Any future reference to the new claims will use their re-numbered claim numbers.

The amendment to the claims filed October 13, 2009 is not in compliance with 37 CFR 1.173(d)(2) because the new claims are not underlined. Correction of the amendment format is required in the response to this Office action.

3. The maintenance fees due at 3.5 years, 7.5 years, and 11.5 years after the issue date of U.S. Patent No. 5,714,460 have been paid, and therefore the reissue procedures are available for this patent.

This reissue application was originally filed within two months of the mailing date of the final judgment of interference 104,553, and therefore the reissue procedures are available for this patent.

4. This application is objected to under 37 CFR 1.172(a) as the assignee has not established its ownership interest in the patent for which reissue is being requested. An assignee must establish its ownership interest *in order to support the consent to a reissue application required by 37 CFR 1.172*(a). The submission establishing the ownership interest of the assignee is informal. There is no indication of record that the party who signed the submission is an appropriate party to sign on behalf of the assignee. 37 CFR 3.73(b).

A proper submission establishing ownership interest in the patent, pursuant to 37 CFR 1.172(a), is required in response to this action.

Papers attempting to establish the consent of assignee to the reissue were filed on November 1, 2004. However, the papers are contradictory. One paper, signed by Timothy R.

Schwartz, PhD., states that Genentech, Inc. is the owner of the entire right, title and interest in and to U.S. Patent No. 5,714,460. A second paper, signed by Paulina Lucrynska (sp.?), states that NeuronZ Limited is the owner of the entire right, title and interest in and to U.S. Patent No. 5,714,460. Two separate legal entities cannot each be the owner of the entire right, title and interest in a single U.S. patent. Further, according to the assignment records of the U.S. Patent and Trademark Office, NeuronZ LTD is the only assignee of record for U.S. Patent No. 5,714,460. Correction is required.

5. Applicant is reminded of the continuing obligation under 37 CFR 1.178(b), to timely apprise the Office of any prior or concurrent proceeding in which Patent No. 5,583,114 is or was involved. These proceedings would include interferences, reissues, reexaminations, and litigation.

Applicant is further reminded of the continuing obligation under 37 CFR 1.56, to timely apprise the Office of any information which is material to patentability of the claims under consideration in this reissue application.

These obligations rest with each individual associated with the filing and prosecution of this application for reissue. See also MPEP §§ 1404, 1442.01 and 1442.04.

6. The reissue oath/declaration filed October 3, 2006 is defective (see 37 CFR 1.175 and MPEP § 1414) because of the following:

The declaration lacks an acceptable duty to disclose statement. Note that the declaration refers only to a duty to disclose as defined by 37 CFR 1.56(a). However, 37 CFR 1.175(a) requires a reissue oath or declaration to comply with the requirements of § 1.63, and § 1.63(b)(3) defines the duty to disclose by reference to all of 37 CFR 1.56. See also MPEP 1414(IV)(C).

Claims 78-92 are rejected as being based upon a defective reissue declaration under 35 U.S.C. 251. See 37 CFR 1.175. The nature of the defect is set forth above.

Forms PTO/SB/51 and PTO/SB/52 are available to help avoid errors like the one indicated above.

7. Claims 78-92 are rejected under 35 U.S.C. 251 as being broadened in a reissue application filed outside the two year statutory period. In particular, the patent claims require the mammal to have actually suffered neural damage. However, the instant claims only require the mammal to be "suspected" of suffering from cerebral ischemia. Because a mammal can be suspected of suffering from cerebral ischemia without actually suffering from cerebral ischemia, e.g., because of the result of a faulty diagnosis or because of the result of a preliminary diagnosis based upon insufficient information, the instant claims embrace the treatment of mammals not embraced by the patent claims, i.e. of mammals suspected of but not actually suffering from cerebral ischemia. Further, the patent claims require a CNS insult which affects glia or other non-cholinergic cells. However, the instant claims do not require the cerebral ischemia to affect glia or other non-cholinergic cells, but rather embrace cerebral ischemia which affects only, e.g., cholinergic cells. Finally, the patent claims require the IGF-1 or biologically active analogue thereof to be administered to the central nervous system of the mammal, whereas the instant claims only require the IGF-1 or biologically active analogue thereof to be administered to the mammal, and not to any particular location in the mammal. A claim is broader in scope than the original claims if it contains within its scope any conceivable product or process which would not have infringed the original patent. A claim is broadened if it is broader in any one respect even though it may be narrower in other respects.

8. Claims 78-92 are rejected under 35 U.S.C. 251 as being based upon new matter added to the patent for which reissue is sought. The added material which is not supported by the prior patent is as follows: The step of identifying a mammal suspected of suffering from cerebral ischemia in new claim 78 is new matter. The original patent does not recite an identifying step and does not recite mammals which are "suspected" of suffering from cerebral ischemia. In the original patent, including column 1, lines 20-60, and column 8, line 65 - column 13, line 45, cited by Applicants as support for the new claim language, there is no identifying step because all mammals discussed therein are known to have suffered central nervous system damage. In the original patent, the mammals are not "suspected" of suffering from cerebral ischemia because all mammals discussed therein are known to have suffered central nervous system damage. The dosage range and the calculation of based upon brain weight of the mammal recited in new claim 80 is new matter. The patent does not recite the dosage range, and does not disclose determining dosages based upon brain weights. Compare, e.g., column 6, lines 1-5, where body weight is used to calculate dosages. The recitation of intrathecal and epidural administration, or of administration by the cerebral vasculature or via the carotid artery, in new claims 82, 83, 85, and 86 is new matter. The patent does not recite such methods of administration. The recitation of ischemia caused by asphyxia, trauma, embolism, thromboembolism, and toxin in new claims 87, 88, and 90-92 is new matter. The patent does not disclose these particular types of cerebral ischemia.

9. Claims 78-92 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention. That subject matter identified as constituting new matter under 35 U.S.C. 251 for the reasons set forth in section 8 above also lacks written description in the original disclosure of the invention, for the same reasons.

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. Claims 78-92 are rejected under 35 U.S.C. 103 as being estopped on the merits by final judgment in Interference No. 104,533. See also 37 CFR 41.127(a) and MPEP 2308.03, Examples 2 and 3 (Rev. 4, October 2005). In the section of the interference count which corresponds to claim 1 of U.S. Patent No. 5,714,460, a mammal suffering from neural damage after a CNS insult is treated with IGF-1 or a biologically active analogue thereof. Claim 3 of the '460 patent, which specifies that CNS insult is ischemic injury, was designated as corresponding to the count. While Applicants moved to designate claim 3 as not corresponding to the count, this motion was denied. See the Decision On Motions, pages 27-29. Thus, the subject matter of claim 3 of the '460 patent has already been held to be patentably indistinct from the count, and this denial provides basis for this determination of interference estoppel. Instant claim 78 differs from claim 3 of the '460 patent in that instant claim 78 does not require the mammal to actually be suffering from cerebral ischemia, but rather only requires the mammal to be suspected of suffering from cerebral ischemia. In this respect, instant claim 78 is broader in scope than claim 3 of the '460 patent, and does not patentably distinguish over the subject matter lost to Applicants in the Interference proceeding. Instant claim 78 also differs from claim 3 of the '460 patent in that instant claim 78 specifies the result of a reduced loss of neurons and/or infarction

associated with cerebral ischemia without significantly altering the brain temperature of the mammal being treated. These results are not specified in claim 3 of the '460 patent. However, instant claim 78 and claim 3 of the '460 patent recite the same method steps using the same compounds directed to the same patients. Because the method steps, compounds, and patients are the same, inherently the method of claim 3 of the '460 patent must produce the same results recited in instant claim 78, and therefore instant claim 78 does not patentably distinguish over claim 3 of the '460 patent. Applicants have not provided any evidence that a significant alteration of brain temperature might be expected upon administration of IGF-1 and/or an analogue thereof, nor have they disclosed any special administration steps which are relied upon in order to avoid a significant alteration of brain temperature. A prior art reference (i.e. the lost count or the subject matter of the claims lost in interference) need not recognize or suggest Applicants' intended results in order to anticipate Applicants' claimed method on the basis of inherency. See, e.g., In re Cruciferous Sprout Litigation, 64 USPQ2d 1202 (CAFC 2002). With respect to instant claims 79 and 84, claims 14 and 15 of the '460 patent recite specific types of administration via the cerebrospinal fluid. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to treat ischemic injury according to claim 3 of the '460 patent by administering the IGF-1 or analogue thereof into the cerebro ventricle or into the lateral ventricle of the brain of the mammal being treated as is also claimed by the '460 patent. See also the Decision On Motions, page 28, lines 9-14. With respect to instant claim 80, the interference count and Applicants' claims lost in interference do not recite the currently claimed dosage. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal dosages for the method of

claim 3 of the '460 patent, because dosage is an art-recognized result-effective variable which is routinely determined and optimized in the pharmaceutical arts. With respect to instant claim 81, the interference count and Applicants' claims lost in interference do not recite treating a mammal who is a human. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to treat a mammal who is human in the method of claim 3 of the '460 patent, because treatment of humans is generically encompassed by the mammals recited in claim 3 of the '460 patent, because one skilled in the art is most motivated to treat ischemia in humans compared to all other mammals, and because there is no evidence that treatment of ischemia using IGF-1 or analogues thereof is significantly different for humans than for other mammals. With respect to instant claims 82, 83, 85, and 86, the interference count and Applicants' claims lost in interference do not recite intrathecal or epidural administration, and do not recite administration via the cerebral vasculature or via the carotid artery. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the IGF-1 or analogues thereof in claim 3 of the '460 patent intrathecally, epidurally, via the cerebral vasculature, or via the carotid artery, because these are known methods of administering drugs to the CNS whereby the BBB is avoided. With respect to instant claims 88 and 89, claim 3 of the '460 patent recites treatment of ischemic injury, claim 4 of the '460 patent recites treatment of traumatic injury, and claim 2 of the '460 patent recites treatment of hypoxic injury. However, the interference count and Applicants' claims lost in interference do not recite treating ischemic injury caused by traumatic injury, and do not recite treating ischemic injury caused by hypoxic injury. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to treat ischemic injury according to claim 3 of the '460

patent when caused by traumatic injury or by hypoxic injury, because treatment of all three types of injuries is claimed by the '460 patent and their treatment was designated as corresponding to the interference count, and because designation of these injuries as a cause or effect would not have been expected to affect the ability of these injuries to be treated in accordance with claims 2-4 of the '460 patent. With respect to instant claims 87 and 90-92, the interference count and Applicants' claims lost in interference do not recite these particular causes of ischemic injury. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to treat ischemic injury according to claim 3 of the '460 patent where the ischemic injury is caused by asphyxia, embolism, thromboembolism, or a toxin, because these are known causes of ischemic injury, because claim 3 of the '460 patent embraces the treatment of ischemic injury regardless of its cause, and because it would be desirable to treat neural damage affecting glia or other non-cholingeric cells regardless of the particular cause of the neural damage.

In the paper titled "Notice Under 37 C.F.R. §1.178(b)" filed June 27, 2003, Applicants refer to footnote 17 of the Decision On Motions in the interference as indicating that Applicants would not be estopped from pursuing in a reissue application narrower claims that would not have been obvious in view of the lost count. However, the basis for this approach is that the reissue claims must be nonobvious over the lost count. As indicated above, current reissue claims 78-92 remain obvious over the lost count and/or are not patentably distinct from the subject matter of the lost claims. Alternatively, the current reissue claims are obvious over the subject matter previously held to be unpatentable to Applicants under 35 U.S.C. 102(g)(1).

12. Claims 78, 79, and 81 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 90/14838. The WO Patent Application '838 teaches treating stroke, i.e.

ischemia, in mammals, including humans, by administering IGF-I or a functional derivative thereof, or by administering IGF-II or a functional derivative thereof. The treatment enhances the survival of neuronal cells which are at risk of dying as a result of the stroke. The active agents are administered parenterally, including intracranially and intraspinally. See, e.g., the Abstract; page 6, lines 18-28; page 12, lines 1-13; page 20, lines 29-35; page 21, lines 1-11, and claim 77. IGF-I functional derivatives, IGF-II, and IGF-II functional derivatives are biologically active analogs of IGF-I. Because the same active agents are being administered to the same mammals according to the same method steps in order to treat the same CNS injuries, inherently the brain temperature of the mammals being treated will not be significantly altered in the method of the WO Patent Application '838 to the same extent claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the method of the WO Patent Application '838 and Applicants claimed method to shift the burden to Applicants to provide evidence that the claimed method is unobviously different than that of the WO Patent Application '838.

With respect to the inherency rejection, note that a prior art reference need not recognize or suggest Applicants' intended results in order to anticipate Applicants' claimed method on the basis of inherency. See Ex parte Novitski, 26 USPQ2d 1389, 1391 (POBA 1993); In re Cruciferous Sprout Litigation, 64 USPQ2d 1202 (CAFC 2002); and more generally MPEP 2112.

See also the Decision On Motions, pages 39-43, in which it was held that all claims of the '460 patent which corresponded to the count were unpatentable over the prior art.

13. Claims 80 and 82-92 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 90/14838. Application of the WO Patent Application '838 is the same as in the above rejection of claims 78, 79, and 81. The WO Patent Application '838 does not teach

Applicants' claimed dosages as set forth in instant claim 80. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal dosages for the method of the WO Patent Application '838 because dosage is an art-recognized result-effective variable which is routinely determined and optimized in the pharmaceutical arts. The WO Patent Application '838 does not teach the particular administration methods recited in claims 82-86. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the active agents of the WO Patent Application '838 by the administration methods recited in instant claims 82-86, because the WO Patent Application '838 is not limited to any particular method of administration (see page 21, lines 1-7), and because the administration methods recited in instant claims 82-86 are known methods of administering drugs to the CNS whereby the BBB is avoided. The WO Patent Application '838 does not teach treating stroke caused by the particular conditions recited in claims 87-92. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to treat according to the WO Patent Application '838 stroke caused by the particular conditions recited in instant claims 87-92, because the WO Patent Application '838 is not limited to the treatment of stroke caused by any particular condition, because the particular conditions recited in instant claims 87-92 are known causes of stroke, and because it would be desirable to enhance the survival of neuronal cells at risk of dying due to the stroke regardless of the particular cause of the stroke.

14. Claims 78, 79, 84, and 89 are rejected under 35 U.S.C. 102(a) as being anticipated by the Gluckman et al article (Biochem. Biophys. Res. Comm. vol. 182, pages 593-599). The Gluckman et al article teaches subjecting rats to inhalational hypoxia, resulting in hypoxic-

ischemic injury, and then administering IGF-1 by cerebroventricular injection to the injured hemisphere. Neuronal loss is reduced, especially in the lateral cortex and in the dentate gyrus. See, e.g., the Abstract and page 595, first full and last paragraphs. Because the same active agent is being administered to the same mammal according to the same method steps in order to treat the same CNS injury, inherently the brain temperature of the mammal being treated will not be significantly altered in the method of the Gluckman et al article to the same extent claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the method of the Gluckman et al article and Applicants claimed method to shift the burden to Applicants to provide evidence that the claimed method is unobviously different than that of the Gluckman et al article.

With respect to the inherency rejection, note that a prior art reference need not recognize or suggest Applicants' intended results in order to anticipate Applicants' claimed method on the basis of inherency. See Ex parte Novitski, 26 USPQ2d 1389, 1391 (POBA 1993); In re Cruciferous Sprout Litigation, 64 USPQ2d 1202 (CAFC 2002); and more generally MPEP 2112.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:00 A.M. to 5:30 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (571) 272-0562. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications

such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jeffrey E. Russel/
Primary Examiner, Art Unit 1654

JRussel
November 12, 2009